



Figure 3.7. Harden and Young's conceptualization of how phosphates might figure in fermentation. Two molecules of glucose would react with two phosphate molecules to create one hexosediphosphate ester and two molecules of alcohol, with the hexosediphosphate slowly breaking back down to glucose and two phosphates, which would then be able to participate in reactions with another molecule of glucose.

they called it a "coferment." Its significance became apparent only in the 1930s (see below).

While researchers investigating alcoholic fermentation were puzzling about the roles of methylglyoxal and phosphates, Gustav Embden was investigating lactic acid fermentation in press juice from muscle. Because adding glucose failed to increase the yield of lactic acid, he proposed that the lactic acid was derived not directly from glucose but from an unknown precursor he designated *lactacidogen* (Embden, Kalberlah, & Engel, 1912). He soon found that adding hexosediphosphate resulted in a large increase in lactic acid and suggested that it was related to *lactacidogen* (Embden & Laquer, 1914; Embden & Laquer, 1921). This work by Embden, together with investigations by Otto Meyerhof (1918) demonstrating that very similar coferments were required in alcoholic fermentation and lactic acid fermentation, pointed strongly to a close connection between the two processes. Meyerhof coined the term *glycolysis* to cover both reaction pathways.

A key to the mysteries surrounding alcoholic fermentation and muscle fermentation was provided by the discovery of two new phosphorus compounds in the late 1920s. The first occurred when Philip Eggleton and Marion Grace Palmer Eggleton (1927) isolated a substance known initially as *phosphagen* and later as *phosphocreatine*. What distinguished this substance was that it rapidly hydrolyzed (i.e., broke down to creatine and phosphate with the consumption of a molecule of water), and released large quantities of energy as it did so. This indicated that it might provide the immediate source of energy for muscle contraction. Eimar Lundsgaard confirmed this hypothesis by showing that in iodoacetate-poisoned rabbits, muscle activity prior